UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUN 23 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: RfD/Peer Review Report of Ethalfluralin (Sonalan) [N-ethyl-N-(2-methyl-2-propenyl)-2,6-dinitro-4-(trifluoromethyl) benzenamine].

CASRN. 55283-68-6
EPA Chem. Code: 113101
Caswell No. 453B

FROM: George Z. Ghali, Ph.D.
Manager, RfD/Quality Assurance Peer Review
Health Effects Division (H7509C)

Rick J. Whitney 6/22/94 for

TO: Joanne Miller, PM 23
Fungicide-Herbicide Branch
Registration Division (7505C)

Lois Rossi, Chief
Re-registration Branch
Special Review and Re-registration Division (7508W)

The Health Effects Division RfD/Peer Review Committee met on March 24, 1994 to discuss and evaluate the existing and recently submitted toxicology data in support of Ethalfluralin re-registration and to re-assess the Reference Dose (RfD) for this chemical.

Material available for review included data evaluation records for a chronic toxicity/carcinogenicity study in rats **(83-5 or 83-1a and -2a)**, a carcinogenicity study in mice **(83-2b)**, a chronic toxicity study in dogs **(83-1b)**, developmental toxicity studies in rats and rabbits **(83-3a and -3b)**, two multi-generation reproductive toxicity studies in rats **(83-4)**, and subchronic toxicity studies in rats, mouse and dogs **(82-1a and -1b)**.

The Committee considered the chronic toxicity study in rats (83-1a, MRID No. 00094776, 92062013) and dogs (83-1b, MRID No. 00153371, 92062014) to be acceptable and the data evaluation records (HED Doc. No. 002251; 005224, 005512) to be adequate. The Committee recommended to revise the no-observable effect level (NOEL) in the rat chronic toxicity study from 4.2 mg/kg/day (the lowest dose level tested) to 32.3 mg/kg/day (the highest dose level

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tested). The Committee also recommended that additional data tables for hematological parameters be included in the data evaluation records of the chronic toxicity study in dogs.

The RfD/Peer Review Committee did not discuss the carcinogenicity phase of the rat study (83-2a, MRID No. 00094776, 92062013) and the carcinogenicity study in mice (83-2b, MRID No. 00094777) in detail. The carcinogenicity issue has already been referred by the respective branch to the Health Effects Division Carcinogenicity Peer Review Committee (HED-CPRC) for weight of the evidence evaluation. The adequacy of the carcinogenicity studies will be judged by the CPRC. However, it should be noted that the no-observable effect level for systemic toxicity in the mouse study was revised to 10.3 mg/kg/day based on additional data submitted.

The Committee considered the recent reproductive toxicity study in rats (83-4, MRID No. 42300301) to be acceptable and the data evaluation record (HED Doc. No. 00000) to be adequate. The older reproductive toxicity study in rats (MRID No. 0094784, 9206219) was judged to be supplementary, though consistent with the recent study, and the data evaluation record for this study (HED Doc. No. 002251) was considered to be inadequate. A new reproductive toxicity test will not be required. The Committee determined that a new reproductive toxicity study would not be expected to affect the Reference Dose for this chemical.

The Committee considered the more recent developmental toxicity study in rats (83-3a, MRID No. 00153370, 92062017) to be acceptable. However, the data evaluation record for this study (HED Doc. No. 005224) was considered inadequate. The data evaluation record (HED Doc. No. 002251) for the older developmental toxicity study in rats (MRID No. 00094783) was considered inadequate and inconclusive to judge the adequacy of the study, additional summary data tables are needed. The data evaluation records (HED Doc. No. 003273; 002251; 002251) of the three developmental toxicity studies in rabbits (83-3b, MRID No. 00129057; 00094781; 00094782) were considered to be inadequate and inconclusive. There was some suggestive evidence of possible developmental toxicity at high dose levels. Additional summary data tables should be included before a final decision can be made regarding these studies. The updated data evaluation records should be submitted to designated Committee members for evaluation.

The RfD for this chemical was first assessed by the Health Effects Division - RfD Committee on November 19, 1986 but has not been submitted to the Agency RfD Work Group for verification. At that time, the RfD was based on a one-year toxicity study in dogs (capsule administration), with a no-observable effect level (NOEL) of 4.0 mg/kg/day. Altered red cell morphology and increased urinary bilirubin were observed at 20.0 mg/kg/day. An uncertainty factor (UF) of 100 was applied to account for the inter-species extrapolation and intra-species variability. On this basis, the

RfD was calculated to be 0.04 mg/kg/day.

In the meeting of March 24, 1994, the Committee recommended that the RfD for this chemical remain unchanged.

It should be noted that this chemical has not been reviewed by the World Health Organization (WHO).

A. Individuals in Attendance

1. Peer Review Committee Members and Associates Present (Signature indicates concurrence with the peer review unless otherwise stated).

William Burnam

Reto Engler

Karl Baetcke

Marcia Van Gemert

Henry Spencer

William Sette

Roger Gardner

Stephen Dapson

George Ghali

Rick Whiting

2. Peer Review Members and Associates in Absentia (committee members and associates who were unable to attend the discussion; signatures (optional) indicate concurrence with the overall conclusions of the committee).

James Rowe

2. Scientific Reviewer (Committee or non-committee members responsible for data presentation; signatures indicate technical accuracy of panel report).

Mike Ioannou

Ray Landolt

3. Others:

M. Morrow, S. Williams-Fay and J. Redden of HED as observers.

CC: Penny Fenner-Crisp
Richard Schmitt
Kerry Dearfield
Marcia Van Gemert
Mike Ioannou
Ray Landolt
James Kariya
Flora Chow
RfD File
Caswell File

B. Material Reviewed

Material available for review included data evaluation records for a chronic toxicity/carcinogenicity study in rats **(83-5 or 83-1a and -2a)**, a carcinogenicity study in mice **(83-2b)**, a chronic toxicity study in dogs **(83-1b)**, developmental toxicity studies in rats and rabbits **(83-3a and -3b)**, two multi-generation reproductive toxicity studies in rats **(83-4)**, and subchronic toxicity studies in rats, mouse and dogs **(82-1a and -1b)**.

1. Adams, E. R. (1981). Two-year dietary evaluation of ethalfluralin in the Fisher 344 rat. MRID No. 92062013, HED Doc. No. 002251. Classification: Core-minimum data. This study satisfies data requirement 83-1a of Subpart F of the Pesticide Assessment Guideline for chronic toxicity testing in rats.

2. Adam, E., and Bernhard, M. (1985). The toxicity of ethalfluralin administered orally to beagle dogs for one year. MRID No. 00153371, 92062014, HED Doc. No. 005224, 005512. Classification: Core-minimum data. This study satisfies data requirement 83-1b of Subpart F of the Pesticide Assessment Guideline for chronic toxicity testing in dogs.

3. Hoyt, J. A., et al. (1992). A 7-month multigeneration bridging study of Ethalfluralin (EL-161, Compound 094961) administered in the diet to Fischer 344 rat. MRID No. 42300301, HED Doc. No. 0000000. Classification: Core-minimum data. This study satisfies data requirement 83-4 of Subpart F of the Pesticide Assessment Guideline for reproductive toxicity testing in rats.

4. Adams, E. R. (1981). A 3-generation reproduction study with Ethalfluralin in the Fischer 344 rats. MRID No. 0094784, 92062019, HED Doc. No. 002251. Classification: Core-supplementary data. This study does not satisfy data requirement 83-4 of Subpart F of the Pesticide Assessment Guideline for reproductive toxicity testing in rats.

5. Robinson, K., et al. (1985). A teratology study of orally administered ethalfluralin (EL-161) in the rat. MRID No. 00153370, 92062017, HED Doc. No. 005224. Classification: Core-Guideline data. This study does not satisfy data requirement 83-3a of Subpart F of the Pesticide Assessment Guideline for developmental toxicity testing in rats.

6. Adams, E. R., et al. (1980). A teratology study with Ethalfluralin in the Wistar rat. MRID No. 00094783, HED Doc. No. 002251. Classification: Core-supplementary data. This study does not satisfy data requirement 83-3a of Subpart F of the Pesticide Assessment Guideline for developmental toxicity testing in rats.

7. Byrd, R., et al. (1983). A teratology study of ethalfluralin (EL-161, Compound 94961) administered orally to Dutch belted

rabbits. MRID No. 00129057, HED Doc. No. 003273. The data evaluation record was considered to be inadequate and inconclusive. The Committee recommended the addition of data summary tables before a final decision regarding the adequacy of the study can be made.

8. Adams, E. R., and Owen, N. V. (1980). A teratology study (I) with ethalfluralin (Compound 94961) in Dutch belted rabbit. MRID No. 00094781, HED Doc. No. 002251. The data evaluation record was considered to be inadequate and inconclusive. The Committee recommended the addition of data summary tables before a final decision regarding the adequacy of the study can be made.

9. Adams, E. R., et al. (1980) A teratology study (II) with ethalfluralin (Compound 94961) in the Dutch belted rabbit. MRID No. 00094782, HED Doc. No. 002251. The data evaluation record was considered to be inadequate and inconclusive. The Committee recommended the addition of data summary tables before a final decision regarding the adequacy of the study can be made.

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Chemical:	**Ethalfluralin**
PC Code:	**113101**
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Memo Date:	**06/23/94**
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HED Records Reference Center
03/08/2002